

Effects of propofol anesthesia induction on autonomic cardiovascular control

G. Dorantes-Mendez¹, F. Aletti¹, N. Toschi², F. Coniglione³, M. Dauri³, M. G. Guerrisi², G. Baselli¹,
M. G. Signorini¹, S. Cerutti¹, M. Ferrario¹

¹Dipartimento di Bioingegneria, Politecnico di Milano, Milano, Italy.

²Medical Physics Section, Faculty of Medicine, University of Rome "Tor Vergata", Roma, Italy

³Anesthesiology Section, Faculty of Medicine, University of Rome "Tor Vergata", Roma, Italy.

Abstract

This paper presents the analysis of the autonomic nervous system (ANS) control and cardiac baroreflex sensitivity in patients undergoing general anesthesia for major surgery, with the goal of evaluating the effects of anesthesia bolus induction with propofol on autonomic control of heart rate (HR) and arterial blood pressure (ABP). The decrease in baroreflex gain observed through two different methods in the LF band suggests that baroreflex responses could be impaired by propofol during anesthesia.

Keywords Baroreflex sensitivity, anesthesia, heart rate variability, blood pressure variability.

1 Introduction

The evaluation of the baroreflex (BR) gain is considered an important tool in clinical practice and gives a valuable measure of cardiovascular (CV) regulation in physiological and disease states, because BR represents the capability of the cardiovascular system to modify heart frequency in response to fluctuations of blood pressure [1].

The identification and quantification of adaptations to anesthetics responses and to surgical maneuvers may be relevant in the prevention of adverse cardiovascular and cardiorespiratory events, which lead to a better patient recovery or increasing survival chances. General anesthetic drugs are known to have direct effects on vascular tone and myocardial contractility, but little is known about how they influence CV regulation of neural and non neural origin, especially considering the potential side effects of general anesthetic agents, which can be serious and potentially life-threatening, particularly in very critically ill patients [2,3].

Despite the importance of understanding the underlying physiological mechanism and its clinical value, few studies in the literature quantify the effect of anesthetic drugs on the alteration of CV control under general anesthesia.

Some authors [4,5] have analyzed baroreflex responses under propofol anesthesia, reporting that

central sympatholytic and/or vagotonic mechanisms enable low heart rate to be sustained despite low blood pressure. These results were interpreted as a “resetting” of the baroreflex, but no impairment of BRS was demonstrated. Other works have reported an inhibition of sympathetic nervous activity in the periphery and a decrease of baroreflex sensitivity in the same conditions [6,7,8,9]. Nevertheless, these studies have been carried out with healthy human volunteers or in minor surgeries with patients classified as ASA (American Society of Anesthesiologists) class I.

In this work, baroreflex sensitivity (BRS) and autonomic control of heart rate (HR) and of arterial blood pressure (ABP) were assessed in patients undergoing general anesthesia for major surgery, in particular, during the bolus induction with propofol. Spectral analysis of HR and ABP variability was carried out as well, in order to determine possible shifts in the sympatho-vagal balance following propofol administration.

2 Methods

A. Data Collection

Custom software was developed (termed “Global Collect”, Labview 2009© environment) in order to simultaneously acquire, interpret and visualize data. All devices perform internal A/D conversion and transmit data (RS232 interfaces) sampled at heterogeneous frequencies and packaged through proprietary protocols. Invasive ABP was measured via an arterial catheter placed in the brachial artery and recorded with the GE S/5 Avance Carestation © at a sample frequency of 100 Hz. Surgeries were performed in the University Hospital Tor Vergata in Rome, Italy. The study was approved by the local Ethics Committee, and the patients gave their written, informed consent to participate.

Data from eight patients undergoing major surgical procedures involving assisted ventilation (5 men and 3 women, age 62.7 ± 9.4 years) were analyzed. Patients patients were not affected either by chronic hypertension or diabetes. Sedation was induced by a bolus of propofol (2mg/kg) and maintained by a total intravenous anesthesia (TIVA, 6-8 mg/(kg hr)).

B. Pre-processing and Data Analysis

Artifact free ABP signals were selected before and after a propofol bolus was administered to induce general anesthesia. In particular, three epochs were considered: 1) awake, i.e. period before induction, when patient is still conscious; 2) sedation, the immediate period after bolus injection; 3) post-intubation, i.e. the immediate period after intubation and concomitant start of mechanical ventilation.

Beat-by-beat series of systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), and pulse pressure (PP), were extracted. Heart period (HP) was assessed as the time interval between two consecutive DAP onsets and was used as a surrogate of RR intervals. The time series were pre-processed with an adaptive filter in order to remove artifacts or ectopic beats. Dickey-Fuller stationary test was employed to select 2 minute long subseries for each ABP derived variables and for each epoch. Beat-by-beat series were then detrended and resampled at 1 Hz, to obtain zero-mean time series. Power spectral density was computed via autoregressive (AR) estimation and power in the high frequency band (HF, $0.15 < f < 0.4$ Hz), low frequency band (LF, $0.04 < f < 0.15$ Hz) and very low frequency band (VLF, $f < 0.04$ Hz) were calculated. BRS was assessed with several techniques, as follows:

a) as power spectral ratio between spectra of SAP and HP, in the LF and HF bands:

$$\alpha_{LF} = \sqrt{\frac{LF_{HP}}{LF_{SAP}}}; \alpha_{HF} = \sqrt{\frac{HF_{HP}}{HF_{SAP}}} \quad (1)$$

when the coherence between the two signals was > 0.5 [10].

b) by means of Transfer Function $H(f)$, with SAP as the input and HP as the output:

$$H(f) = \frac{S_{xy}(f)}{S_{xx}(f)} \quad (2)$$

where $S_{xx}(f)$ is SAP spectrum and $S_{xy}(f)$ is the cross spectrum between SAP and HP [11]. The average gain of the transfer function between SAP and RR was estimated in the frequency range where the coherence is high (≥ 0.5) in LF (BRS TF LF) and HF band (BRS TF HF).

c) by means of the sequence method, which consists in identifying the sequences in which HP and SBP simultaneously increased (up sequence) or decreased (down sequence) over three or more beats. Both up and down sequences were considered baroreflex sequences if they consist at least of three consecutive beats exhibiting SAP-HP correlation higher than 0.8; additionally SAP and HP beat-to-beat changes must be at least of 1 mmHg and 4 ms, respectively [12]. For each baroreflex sequence the regression slope was estimated using linear regression analysis and all slopes were averaged to obtain the index of the baroreflex sensitivity.

One-way analysis of variance (ANOVA) for repeated-measure and then post-hoc comparisons test were performed for each index. The comparison

between epochs was determined with Student's paired t-test or Wilcoxon signed-rank test according to data distribution. Statistical significance was considered for two tailed p-values < 0.05 .

3 Results

A significant decrease in the mean values of SAP, DAP, MAP and PP during propofol induction and after the intubation was obtained with respect to awake period, mainly due to the vasodilator effect of the anesthetic agent (table 1). The mean value of HP did not show significant changes either after propofol induction or after intubation.

Figure 1 shows the power spectral density (PSD) of HP and DAP variability series in a patient: an evident reduction in PSD after the propofol administration, and a marked respiratory peak during post-intubation epoch can be observed. Total power significantly decreased in HP, DAP and MAP time series from awake to both sedation and post-intubation epochs, while total power of SAP and PP signals showed only a significant decrease in post-intubation epoch in comparison with awake period (table 2).

A significant decrease of LF and HF power was observed in sedation and post-intubation epochs in comparison with awake in HP and DAP variability series. As regard to SAP variability signals, a significant decrease in LF band in post-intubation epoch only was obtained (table 2).

HF% of HP and SAP reported significant higher values in post-intubation epoch with respect to awake period; while no significant difference was reported in DAP variability series. LF% reported significant lower values during post-intubation epoch in comparison with awake in HP and SAP fluctuations time series.

As compared to awake, the BRS assessed by α index showed a significant decrease after sedation for the LF band. A significant decrease in sedation and post-intubation epoch was obtained as well by BRS estimated by TF method (figure 2).

No significant changes of BRS in HF band were reported during sedation epoch. The sequence method did not show any significant differences amongst the three epochs.

Table 1. Heart Period and Blood Pressure average values for each epoch

	Awake	Sedation	Post-intubation
HP (bpm)	69.5 ± 13.2	67.1 ± 13.0	65.3 ± 10.4
SAP (mmHg)	147±20.5	113±25.2*	110±27.8*
DAP (mmHg)	70.2±10.7	60.2±8.5†	57.6±8.6†
MAP (mmHg)	97.1±11.5	78.2±12.1*	76.4±15.1*
PP (mmHg)	76.4±20.3	53.0±20.9*	52.5±23.4*

Values are expressed as mean ± std.

† Student t-test p value < 0.05 (vs awake)

* Student t-test p value < 0.01 (vs awake)

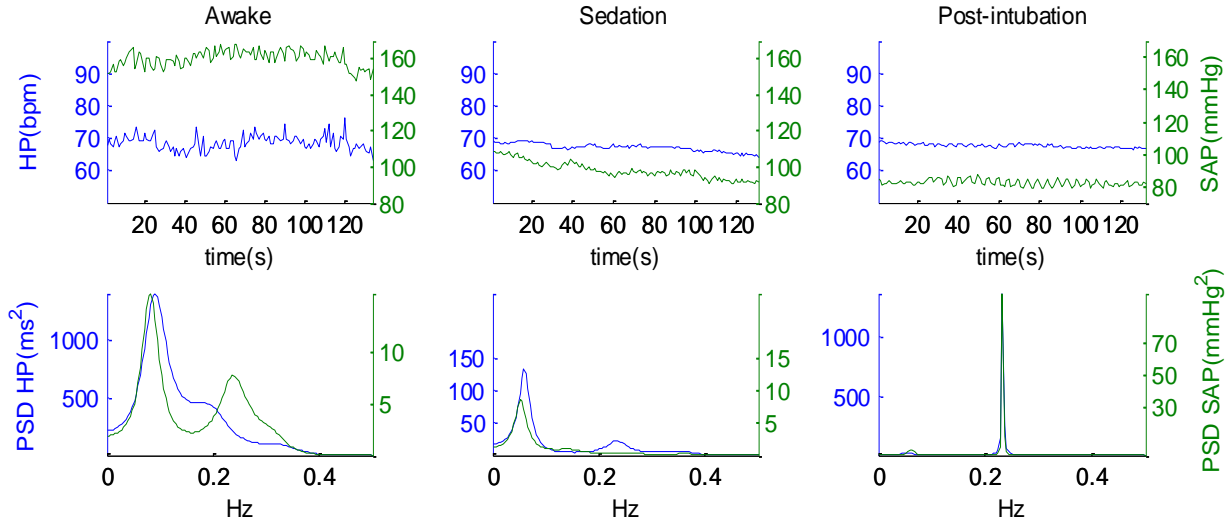


Figure 1: HP and SAP time series and spectra of a single patient during awake, sedation and post-intubation epochs. Blue line and axes refer to HP signal; green ones to SAP signal.

Table 2. Power Spectral indices of HP, SAP and DAP variability time series

	Awake	Sedation	Post-intubation
HP			
LF(ms ²)	42075±29915	13629±25090*	4313±3841*
HF(ms ²)	22174±19837	6915±8410*	3963±2954*
LF%	68.2±15.9	58.9±13.7	42.5±26.2*
HF%	31.5±15.9	40.0±13.2	56.7±26.0*
LF/HF	2.8±1.6	1.7±0.9	1.3±1.4*
TP(ms ²)	72079±45311	25085±42716*	9389±6094*
SAP			
LF(mmHg ²)	517.0±318.3	328.5±469.9	136±190*
HF(mmHg ²)	594±968	326±735*	142.6±72.6
LF %	61.5±21.3	70.1±17.7	36.8±21.3*§
HF %	38.3±21.3	29.6±17.8	63.0±21.3*§
LF/HF	2.3±1.5	3.3±2.0	0.8±0.9*§
TP(mmHg ²)	1133±1138	733±1183	294±249*
DAP			
LF(mmHg ²)	290±189	105±147*	47.7±68.1*
HF(mmHg ²)	342±700	155±408*	28.0±13.9*
LF %	66.2±22.9	72.4±23.7	50.4±21.9
HF %	33.6±22.9	27.5±23.7	49.5±21.9
LF/HF	3.2±2.4	5.9±5.7	1.5±1.4§
TP(mmHg ²)	665±812	285±532*	82.2±83.2*

Values are expressed as mean ± std
 Wilcoxon signed-rank test * p-value < 0.05 (vs awake)
 Wilcoxon signed-rank test § p-value < 0.05 (vs sedation)

4 Discussion and Conclusions

The present study investigated the effects of propofol anesthesia in autonomic cardiovascular control. As expected, a significant decrease of ABP average values was obtained, which can be explained by the vasodilatory effect of propofol.

No changes in HP average values resulted by propofol induction, a finding similar to previous works [13, 14]. The maintenance in heart rate may depend also to the anesthetic dose. Indeed, Xu et. al. [15] reported that propofol mediated sympathetic depression in nerve-intact animals requires a high dose of agent, whereas in intact and vagotomy animals, heart rate did not significantly change with a lower dose of anesthetic.

Our results reported a significant decrease in LF power in DAP and SAP variability time series during sedation and post-intubation epochs (table 2). As ABP LF power reflects sympathetic activity on peripheral resistance, these results suggest that propofol induction may reduce sympathetic nervous modulation of peripheral vasculature, and this is consistent with the results reported by Ogawa [16] and with the attenuation in peripheral sympathetic outflow reported by Sellgreen [6].

As regard the fluctuations of HP, total power, LF and HF components decreased significantly after induction. Despite an unaffected average HP value, these analyses hint an attenuation of cardiac autonomic regulation induced by propofol anesthesia.

The BRS analysis showed a reduction of baroreflex gain in the LF band from awake to sedation and post-intubation epochs. This may suggest that the baroreflex responses and autonomic control were blunted to control HP at lower ABP values during the preparatory phase of surgical intervention, i.e. induction and sedation phase.

In this study we have not considered the influence of respiratory input in the BRS analyses. However in future studies it could be interesting to include the respiratory activity, because it is well known that respiration also modulates heart rate trough the respiratory sinus arrhythmia mechanism [9]. Moreover, during positive mechanical ventilation the respiratory oscillations can mask ANS modulation and its effects should be filtered.

These are preliminary results inherent to the effects of propofol induced anesthesia in patients not affected by chronic hypertension and diabetes. Further analyses are

still ongoing in particular with patients affected by chronic hypertension and diabetes, in order to study the influences of pathological alteration in autonomic and ABP control on the response to propofol induced anesthesia.

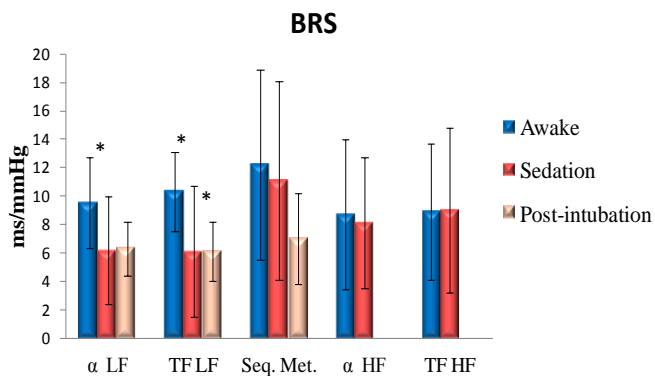


Figure 2: BRS assessed by α index, Transfer Function (TF) in LF and HF bands, and Sequence method during awake, sedation and post-intubation epochs. * marks significant differences (t-test p-value <0.05) with respect to awake epoch. In post-intubation period BRS in HF band was excluded due to mechanical ventilation affecting respiratory band.

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Address for correspondence:

Guadalupe Dorantes Méndez
Politecnico di Milano
guadalupe.dorantes@mail.polimi.it